REMARKS

The Office Action

Claims 29-50 were rejected under 35 U.S.C. § 112, second paragraph. This rejection is addressed as follows.

New Claims

New claims 51 and 52 have been added to include subject matter of claims 33 and 39, respectively. New claim 53 has been added to indicate that the positive and negative makers of claim 47 are DNA probes, and new claim 54 has been added to incorporate cancelled subject matter of claim 49. No new matter has been added by addition of these new claims.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 29-50 were rejected under § 112, second paragraph as being indefinite on several grounds, which are addressed as follows.

Claim 29 was deemed indefinite in reciting the phrase "in vivo assay." This rejection has been met by the present amendment in which the phrase "in vivo" has been deleted from the preamble of the claim.

In addition, applicants point out that claim 29 has been amended to include new step (a), which requires "providing a suspension of isolated or expanded cells and determining markers thereof." It is submitted that this step was implicit in the claim as filed and would have been understood by the skilled person. Accordingly, incorporation of this language does not constitute new matter.

Claim 29 was also deemed incomplete for omitting essential elements, with the Examiner asserting that claim 29 must specify both "a selecting cells identified with desired positive molecular markers" and "a step for purifying the cells selected for further evaluation and use." On these issues, applicants point out that such steps are

unnecessary. Cells used in the method of claim 29 are not selected prior to injection in an animal. Indeed claim 29 relates to the use of the animal for identifying positive and negative cell markers. A number of expression markers of the cell suspensions of chondrocytes are identified prior to introducing the cells into an animal and, based on the outcome of step (d) (evaluating the *in vivo* formed cartilage histologically as to whether it is stable, non-vascularised cartilage) the markers positively or negatively associated with the ability of the population to form stable hyaline cartilage are identified. Thus, the markers that appeared in those cell populations that form stable hyaline cartilage in vivo are considered positive markers, while those markers that did not appear in the cell populations that turn out to form stable hyaline cartilage, are considered negative markers. Finally, applicants note that a correlation step describing how step (e) relates to the preamble phrase "identifying molecular markers linked to phenotypic stability of a chondrocyte cell population" is unwarranted. This is because chondrocyte populations with/without chondrocyte phenotypic stability (i.e. non-selected chondrocyte populations) are used in order to identify the markers which are linked to chondrocyte phenotypic stability.

Another basis of the indefiniteness rejection turns on the assertion that the phrase "in an amount equivalent to" does not recite "at least 1 x 10^6 chondrocytes," rendering the claim indefinite because the meaning of the phrase "in an amount equivalent to" cannot be determined. This ground of the rejection is respectfully traversed. Applicants first point out that the phrase "in an amount equivalent to" should not be taken out of context. Next, like the claims, applicants' specification, for example, at page 15 (lines 4-5), indicates that the suspension of chondrocytes is "in an amount equivalent to at least 1 x 10^6 ... chondrocytes as applied to immune-deficient mice." Moreover, one skilled in the art would further understand that the required number of cells is that amount of cells that allows for the production of stable, non-vascularized cartilage. Accordingly, given this description, one skilled in the art would readily understand the meaning of the phrase "in an amount equivalent to," and as such, this description "reasonably apprises those

skilled in the art" of the scope of the present claims. See, for example, Miles Laboratories, Inc. v. Shandon, Inc., 997 F.2d 870, 27 U.S.P.Q.2d 1123 (Fed. Cir. 1993) ("If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more...The degree of precision necessary for adequate claims is a function of the nature of the subject matter."). Reconsideration on this point is requested.

Claim 30 was deemed unclear in reciting the phrases "using freshly isolated or serially passaged cells using ..." This rejection has been met by amending claim 30 to recite "using freshly isolated or serially passaged cells and using differential gene expression analysis ..."

Claim 30 was also deemed indefinite in view of the phrase "methods including." This rejection has been met by the present amendment to claim 30, which replaces "including" with the phrase "selected from the group consisting of."

Another basis of the indefiniteness rejection is based on the assertion that the phrase "and/or markers co-detectable with these markers and/or reporter ..." is indefinite because the metes and bounds intended cannot be determined. To address this issue, all occurrences of the phrase "co-detectable with these markers" has been amended to indicate that such markers are "identified by the method of claim 29." Accordingly, as amended, the phrase "co-detectable markers" relates to those markers that are found in the method of claim 29 to be co-expressed with the markers recited in claim 31.

With respect to claim 31, applicants also point out that this claim has been amended to specify that a reporter construct utilized in the claimed method includes the promoter of the marker itself. Support for this amendment is found, for example, in the specification on page 15 (lines 3-8), page 15 (lines 12-15), and page 21 (lines 11-15). All other claims including this language have been similarly amended.

Claim 33 was deemed indefinite for reciting the phrase "hybridizing to messenger RNA cells," as well as for omitting essential elements. In response to this rejection, it is first pointed out that the claimed method does not include the step of selecting cells

identified by markers, as the method relates to identifying cells using markers. To clarify the steps of the claimed method, claim 33 has been amended. In particular, step (b) has been included, which relates to "identifying cells that (i) hybridize with the positive markers and (ii) do not hybridize with the negative markers for chondrocyte phenotypic stability." Support for this amendment is found in applicants' specification, for example, on page 18 (lines 30-34) and also on page 21 (lines 2-6).

Claim 33 was also deemed indefinite for omitting a reference to "probes." To address this issue, claim 33 has been amended to indicate that the probes are positive and negative markers for chondrocyte phenotypic stability.

Claims 39 and 40 were deemed indefinite in omitting essential elements. To address this rejection, claim 39 has now been amended to include the steps of claim 33 and claim 40 has been amended to include the steps of claim 35. Applicants further note that claim 40 clearly identifies the selection of cells based on the expression of positive or negative markers.

Claim 41 was deemed indefinite for reciting multiple preambles. Claim 41 has been amended so that it no longer recites multiple preambles, as well as to include the steps of claim 29.

Claims 43 and 44 were deemed indefinite because the claim limitations are not present in a single sentence and for lacking sufficient antecedent basis. To address these issues, claims 43 and 44 have been amended to relate to "a method of transplanting" and to provide sufficient antecedent basis for the recitation of "said," as suggested by the Examiner.

Claim 47 was deemed indefinite on the grounds that reference to claim 33 does not describe how to identify cells with chondrocyte phenotypic stability and that the claim fails to recite a correlation step between identifying desired cells and hybridizing to messenger RNA from cells, sets of DNA probes provided on DNA arrays or DNA chips." To address this issue, applicants have amended claim 47 to refer to a composition that includes the molecular markers identified according to claim 29.

Finally, claims 49 and 50 were deemed indefinite in reciting a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. This rejection has been met by the present amendment.

Applicants note that the present amendments were solely made to expedite prosecution and applicants reserve the right to pursue the subject matter of the canceled claims or subject matter in this or a continuing application.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 5 January 2005

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